



Drugs Acting on the Cardiovascular System.

Drugs on C.V are classified into

1. Drugs acting on the heart; stimulants and depressants.
2. Drugs acting on blood vessels; vasoconstrictors and dilators
3. Drugs acting on blood; antihaemorrhagics, coagulants and anticoag.

Drugs acting on the heart.

I Cardiac Stimulants

1. Cardiac glycosides as Digitalis.
2. Theophylline
3. Sympathomimetics
4. Epinephrine

II. Cardiac depressants:

1. Direct myocardial depressants;
2. Parasympathomimetics
3. Sympatholytics

Cardiac Glycosides

These are glycosides from Digitalis, Strophanthus and Squill.

They are powerful myocardial stimulants and are of value in heart failure.

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Digitalis

leaves of *Digitalis purpurea*, and *Lanata* (Foxgloves) give the glycosides digitoxin, gitalin and digoxin.

Pharmacological actions:

I. Cardiovascular actions:

1. Increase the force of systolic contraction increasing cardiac output, by direct myocardial action
2. Decrease heart rate by reflex stimulation of the vagus center through baroreceptors and by direct delay of conduction in S.A and A.V nodes
3. Change E.C.G. prolonging P-R and shorten Q-T, depressing RST and T diminished or inverted.
4. Diuresis decreasing B.L. volume by improving circulation

* ... Cumulative resulting in: arrhythmia, anorexia, vomiting and diarrhoea. Stop the drug, K, Atrop. metab.

II. Diuretic action.

It is secondary to improved circulation, increasing the cardiac output and glomerular filtration. It suppress aldosterone decreasing Na inducing diuresis

Mechanism of Action:

Cardiac glycosides act by direct myocardial stimulation by stimulating Na/K ATPase enzyme, Na enters releasing Ca ions which become available to contractile protein converting chemical energy into work without extra need to O_2

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Therapeutic uses of Digitalis:

1. Treatment of CHF (congestive heart failure)
2. Controlling atrial fibrillation before Quinidine.

Strophanthus

Similar to digitalis. Its active principal is Strophanthus G or Ouabain given i.v for rapid action

Squill

The bulb includes the glycoside Scillarin A & B.
Resembles digitalis but less active used as expectorant

Antiarrhythmic Drugs.

Drugs used for treatment of cardiac arrhythmias includes:

I. Na channel blockers: Quinidine - local anesthetic

1. Quinidine,

Alkaloid from Cinchona bark acts by direct depressant action on myocardium by reducing the rate of depolarisation by rendering it less permeable to Na inducing:

- a. Depress myocardial excitability
- b. Slows the conduction in AV node
- c. Depress myocardial contractility specially auricles
- d. It restores normal cardiac rhythm in cases of fibrillation or atrial flutter. A normal ECG with prolonged P-R and wider QRS is also recorded.

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2. Local anaesthetics

These act with a quinidine like action.

a. Procainamide

b. lidocaine, lignocaine, xylocaine

These are used in ventricular arrhythmias after mild infarctions.

II. Beta blockers

These block β_1 receptors in the heart suppress the pacemaker with a quinidine like action. These include:

Propranolol (Non selective)

Practolol - Atenolol (Selective β_1 blockers)

III Potassium channel blockers

This includes Bretylium which blocks K channel inhibiting depolarization prolonging the action potential.

IV Calcium channel blockers

Verapamil, Nifedipine, Diltiazem: these inhibit Ca influx in heart muscle and vessels reducing their contraction with a slow ventricular response to atrial fibrillation

* These drugs reduce cardiac contractility used to reduce B.L. pressure and as Antiangina.

Drugs acting on Blood vessels

A These include general arterial and venous dilators.

1. Nitrites and Nitrates

2. Papaverine

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3. Xanthine derivatives
4. Nicotinic acid (Niacin)
5. Aminophylline.

Nitrites and nitrates

a. Nitroglycerine b. Isosorbide mono-dinitrate.

Absorbed rapidly induce bl. vessels and coronary relaxation decreasing bl. arterial resistance and reduce venous tone. This is by releasing Nitric oxide. It is used to reduce bl. pressure and dilate the coronaries.

- Na nitroprusside (Nipride)

It directly relaxes arterial and venous muscles decreasing cardiac preload.

These are used in

- 1) congestive heart failure CHF
- 2) Angina pectoris
- 3) Hypertension
- 4) Pulmonary high pressure
- 5) Bleeding in surgery.

Arterial vasodilators

Hydralazine directly relaxes arteriolar smooth muscles decreasing arterial bl. pressure used in

- a. Treatment of hypertension
- b. Treatment of CHF
- c. Treatment of hypertension due to renal impairment.

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Ant. Vaso constrictors

1. These are peripheral bl. vessels constrictors increasing the blood pressure which act by stimulating Vaso motor Center.
 - a. Direct:
Caffeine - Paraldehyde, Amphetamine, Nikethamide.
 - b. Indirect: through chemoreceptors as
Lobeline
2. Drugs stimulating the sympathetic nerve supply
Adrenaline, Ephedrine, Norach., Amphetamine.
3. Drugs directly stimulate vascular muscular wall
Ergotamine.

Drugs Acting on Blood

These are two groups of drugs including

1. Antianemics and Antileukemics
2. Coagulants and Anticoagulants.

Antianemic Drugs:

1. Hemorrhagic anaemia

That is treated by blood transfusion and iron rich foods

2. Microcytic anaemia

That is due to iron deficiency. Treated by iron preparations

- a. Ferrous salts for large animals (Sulphate, Phosphate...)
- b. Soluble preparations for small animals (Iron ammonium citrate, iron quinine citrate)

c. Ferric iron to be injected i.v. in animals unable to absorb iron.

3. Macrocytic anaemia (Pernicious anaemia)

That type is due to deficiency of the intrinsic factor (mucoprotein) in the stomach or Vit B₁₂ deficiency (Cyanocobalamin)

It is treated by Vit B₁₂ or Folic acid

4. Aplastic anaemia

That is due to depression of bone marrow by poisons, radioactive substances. It is treated by removing the causative agent and Vit B₁₂ supply with iron.

5. Hemolytic anaemia.

It is due to destruction of red cells by bacteria, parasites, or toxins, treated by removing the cause and Vit B₁₂ with iron supply.

Antileukemic drugs

Leukemia is a form of Cancer of the white cells.

It is treated by Antineoplastic drugs:

Alkylating agents (Cyclophosphamide)

Antimetabolites (Methotrexate).

Coagulant Drugs.

Blood coagulation is completed by prothrombin from Vit K transformed to thrombin in presence of Ca. Thrombin helps the conversion of fibrinogen to fibrin which forms a

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network trapping the agglutinated platelets by thrombin forming the blood clot.

* Coagulant drugs help the rapid formation of the clot to stop bleeding or haemorrhages

1- Local anticoagulants: drugs which precipitate proteins as Ferric chloride, tannic acid, Alum, Ca aglnate are used as styptics

2- Systemically:

a. Vit K. watery or oily or Synthetic Menadione bisulphate (KonaKion) injected i.m is of value.

b. Calcium salts: gluconate, lactate or Chloride (2-5%) injected s.c or i.v

Anticoagulant Drugs:

These are drugs which delay blood coagulation in vivo or in vitro. These are valuable in

a. Bl transfusion

b. Treatment of thrombosis

c. Preserving blood samples.

In Vitro anticoagulants

Oxalic acid 0.1%, Na or K oxalates or Disodium EDTA or Na Fluoride unit with bl. Calcium preventing its coagulation

Na Citrate 0.4% reduces the Ca ionization so can be used in vitro and in vivo in blood transfusion

Heparin can be used in vitro for bl. preservation

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In vivo anticoagulants

1- Heparin.

Heparin acts as anticoagulant *in vitro* and *in vivo* by interfering with the conversion of prothrombin to Thrombin preventing thrombin from acting on fibrinogen to fibrin.

It also prevents the coagulation and agglutination of bl. platelets by decreasing thrombin.

It is given i.v produces its effect in 10 minutes and is destroyed by the heparinase enzyme in few hours.

Heparin antidote is Protamine Sulphate

2. Dicoumarol (Dicoumarin)

It is an oral anticoagulant chemically related to Vit K. It acts only *in vivo* by reducing prothrombin in liver preventing the use of Vit K. It also reduces the adhesiveness of bl. platelets and converts to salicylic acid acting as anticoagulant 1-2 days and lasts for 3-7 days, not effective in emergency.

Dicoumarin antidote is Vit K i.v

3. Warfarin Na

It is anticoagulant similar to dicoumarol that antagonise Vit K. *It is used as Rodent cide.